

### REMARKS

Entry of this amendment, and reconsideration of this application, as amendment, are respectfully requested.

Claims 29-40 and 42-50 were rejected under 35 U.S.C. §103(a) over Alfano in view of Dukor. Claim 41 was rejected under 35 U.S.C. §103(a) over the Alfano, Dukor and Corenman. Applicants respectfully traverse each of these rejections.

The presently claimed invention discloses methods and apparatus for *in vivo* detecting and characterizing conditions in abnormal tissues that present in vascular diseases, in particular, atherosclerosis, by using reflection-based mid-infrared (IR) spectroscopy. Specifically, the presently claimed invention teaches the use of signature mid-IR spectral bands as diagnostic marker for atherosclerotic disease. Those signature bands are set forth in the amended claim 29.

In contrast, Alfano fails to teach or suggest the use of claimed signature mid-IR spectral bands to diagnose atherosclerosis. The Examiner alleges that Alfano discloses the wavenumbers 1659 cm<sup>-1</sup> and 957 cm<sup>-1</sup>, which fall within the claimed mid-IR spectral band range. Applicants respectfully submit that the Examiner misinterprets Alfano.

In the presently claimed invention, those signature bands are from reflectance spectra. In abnormal tissues, increased absorbance peaks at those selected wavenumbers are observed. In contrast, the wavenumbers 1659 cm<sup>-1</sup> and 957 cm<sup>-1</sup> described by Alfano are not from reflectance spectra, but are Raman bands at Raman Shifts. Raman Shifts don't refer to absorbance peaks at specific wavenumbers at all, but are indicators of light shift, i.e., the difference between wavenumbers. See, for example, col. 7, line 68-col. 8, line 13 ("... $\nu_1$  and  $\nu_2$  are the wavenumbers of two different Raman shifts....one can determine if a human aortic tissue sample is calcified atherosclerotic tissue either by noting the presence of light shifted by 957 cm<sup>-1</sup>...). Furthermore, the formula to calculate Raman shift is

$$\Delta w = \left( \frac{1}{\lambda_0} - \frac{1}{\lambda_1} \right), \text{ where } \Delta w \text{ is the Raman shift expressed in wavenumber, } \lambda_0 \text{ is}$$

the excitation wavelength, and  $\lambda_1$  is the Raman spectrum wavelength. (See [http://en.wikipedia.org/wiki/Raman\\_spectroscopy](http://en.wikipedia.org/wiki/Raman_spectroscopy)).

As explained above, although Raman shift is expressed in the format of a wavenumber, it does not refer to reflectance or absorption at a specific wavenumber at all. Therefore, the wavenumbers  $1659\text{ cm}^{-1}$  and  $957\text{ cm}^{-1}$  described by Alfano have entirely different meanings from the wavenumbers claimed in the present invention. Thus, Alfano does not teach or suggest the use of the claimed signature mid-IR spectral bands to diagnose atherosclerosis at all.

The deficiencies of Alfano are not overcome by either Dukor or Corenman.

Moreover, as explained in previously submitted Rule 132 declaration of inventor Hoi-Ying Holman, Dukor merely discloses a method and system for diagnosing carcinoma by using IR spectroscopy, NOT reflective IR spectroscopy as in the presently claimed invention. In addition, Dukor does not teach or suggest using the reflective IR spectroscopy technique to diagnose atherosclerosis. Due to the huge difference between carcinoma tissue and atherosclerosis tissue, the reflective IR spectroscopy as in the presently claimed invention can't be applied to carcinoma diagnosis. Thus, a skilled artisan would not have combined Alfano and Dukor to arrive at the present invention.

Therefore, all §103(a) rejections should be withdrawn.

In view of the foregoing allowance is respectfully requested.

The Commissioner is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 50-0624, under Order No. NY-LBNL-238-US.

Respectfully submitted

FULBRIGHT & JAWORSKI L.L.P.

By /James R. Crawford/  
James R. Crawford  
Reg. No. 39,155

666 Fifth Avenue  
New York, New York 10103  
(212) 318-3148